General

Guideline Title

Community management of opioid overdose.

Bibliographic Source(s)

World Health Organization (WHO). Community management of opioid overdose. Geneva (Switzerland): World Health Organization (WHO); 2014. 74 p. [133 references]

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The definitions for the strength of the recommendations (strong, conditional) and the quality of evidence (high, moderate, low, very low) are provided at the end of the "Major Recommendations" field.

Recommendation 1

People likely to witness an opioid overdose should have access to naloxone and be instructed in its administration to enable them to use it for the emergency management of suspected opioid overdose. (Strength of recommendation: Strong; Quality of evidence: Very low)

Remarks

- There may be both legal and policy barriers to the access and use of naloxone by lay first responders, which may need to be reviewed in order to implement this recommendation.
- In addition to the use of naloxone, emergency care of suspected opioid overdose should include ventilation support, airway management and management of withdrawal effects (specific emergency-care measures are described in Recommendation 3). While comprehensive training in opioid overdose and resuscitation is desirable, basic training can enable the effective emergency use of naloxone and the lack of more extensive training should not impede its use in the community. There are many training programmes available reflecting local contexts and needs.
- The panel notes that the people at risk of overdose and those likely to witness an overdose may vary according to the local context (see examples in the table below).
- Access to naloxone implies that the price remains affordable. The Guideline Development Group (GDG) made a strong recommendation for

the use of naloxone based on current prices but note that this could change if prices rise drastically.

Decision on Strength of Recommendation

The GDG determined that this recommendation should be strong despite the very low quality evidence due to the life-saving nature of the intervention and the apparent absence of significant harm. The panel also noted that this is a feasible intervention, highly valued by those at risk of opioid overdose and those likely to witness an opioid overdose in the community.

Table: Examples of People at Higher Risk of Overdose and People Likely to Witness an Overdose

People at higher risk of overdose	• People with opioid dependence, in particular those with reduced tolerance (following detoxification, release from incarceration, cessation of treatment) • People who inject opioids • People who use prescription opioids, in particular those on higher doses • People who use opioids in combination with other sedating substances • Opioid users with other significant medical conditions (human immunodeficiency virus [HIV], liver or lung disease, depression) • Household members of people in possession of strong opioids
People likely to witness an overdose	• People at risk of an opioid overdose, their friends and families • People whose work brings them into contact with people who overdose (health care workers, police, emergency service workers, people providing accommodation to people who use drugs, peer education and outreach workers)

Recommendation 2

Naloxone is effective when delivered by intravenous (IV), intramuscular (IM), subcutaneous (SC) and intranasal routes of administration. Persons using naloxone should select a route of administration based on the formulation available, their skills in administration, the setting and local context. (Strength of recommendation: Conditional; Quality of evidence: Very low)

Remarks

Route of Administration

- The GDG recognizes that the IV route is appropriate and effective in medical settings.
- Parenteral use of naloxone (IV, IM, SC) requires sterile injection equipment.
- The capacity of the nasal mucosa to absorb liquids is limited, so if the intranasal route of administration is to be used, concentrated forms of naloxone should ideally be used.
- The GDG has made this recommendation fully aware that the intranasal route is currently an off-label (non-licensed) route.
- Affordability may dictate the preferred route in particular contexts.

Dosage

- The choice of initial dose will depend on the formulation of naloxone to be used and the context.
    - In medical settings dose selection is not generally an issue as dose titration is standard practice. In non-medical settings dose titration is not so easily accomplished and higher initial doses may be desirable.
    - The context also dictates the total amount of naloxone made available to non-medical responders. More than one dose may need to be available in a non-medical setting. The initial dose should be 0.4 mg–2 mg, targeting recovery of breathing. In most cases 0.4–0.8 mg is an effective dose. It is important to provide sufficient naloxone to supplement the initial dose, as necessary.
    - Intranasal delivery may require a higher dose. It should be noted that the commonly used method of intranasal administration is to spray 1 ml of the 1 mg/ml formulation of naloxone into each nostril with an atomizer connected to a syringe.
- Where possible, efforts should be made to tailor the dose to avoid marked opioid withdrawal symptoms. The GDG notes that higher initial doses above 0.8 mg IM/IV/SC are more likely to precipitate significant withdrawal symptoms.
- A more complicated situation arises where there has been an overdose of a combination of drugs. In this situation naloxone is still beneficial

for reversing the opioid intoxication component of the overdose.
- It is essential that expert professional assistance be sought as soon as possible. Even in the case of opioid overdose, a person may not respond to naloxone if other drugs have been taken.

Decision on Strength of Recommendation

The GDG decided to make this a conditional recommendation because, while there was certainty that the benefits outweighed the harms and that the end-users favoured this recommendation, there was uncertainty about the costs of intranasal naloxone, as this is currently an "off-label" use.

Recommendation 3

In suspected opioid overdose, first responders should focus on airway management, assisting ventilation and administering naloxone. (Strength of recommendation: Strong; Quality of evidence[1]: Very low)

Remarks

Because the key feature of opioid overdose is respiratory arrest, ventilation is a priority. While recognizing there are different protocols in different parts of the world, the GDG suggests the following steps in resuscitating an individual with suspected opioid overdose.

- Apply vigorous stimulation[2], check and clear airway, and check respiration – look for chest rising and falling.
- In the presence of vomit, seizures or irregular breathing, turn the patient on their side, and, if necessary, clear the airway of vomit.
- In the absence of regular breathing provide rescue ventilation and administer naloxone.
- If there are no signs of life, commence chest compressions.
- Re-administer naloxone after two to three minutes if necessary.
- In all cases call for professional assistance.
- Monitor the person until professional help arrives.
- Where available, cardiopulmonary resuscitation (CPR) mouth barriers should be used for rescue ventilation.

Decision on Strength of Recommendation

The GDG determined that the recommendation should be strong despite the very low quality of the evidence because of the life-saving nature of CPR, including rescue breathing, in suspected opioid overdose in the community, and the low likelihood of resuscitation-induced harm. The panel also noted the feasibility of, and strong preferences in favour of CPR, including rescue breathing, expressed both by those at risk of overdose and those likely to witness an opioid overdose.

[1]The quality of evidence refers to the clinical trial evidence on the key question (comparing different approaches to resuscitation in opioid overdose) rather than the clinical trial evidence for resuscitation *per se*.

[2]The most common way of applying vigorous physical stimulation to someone who is not responding to verbal stimulation is to rub the person's sternum (breast bone) with one's knuckles.

Recommendation 4

After successful resuscitation following the administration of naloxone, the affected person should have their level of consciousness and breathing closely observed until they have fully recovered. (Strength of recommendation: Strong; Quality of evidence: Very low)

Remarks

- This recommendation is made with knowledge of the extended duration of opioid overdose, especially with the variety of longer-acting opioids and opioid formulations in current usage. It is critical to appreciate that the witness cannot tell what the length of action will be without observing the person who has overdosed. It is important to increase awareness of the need to remain with the person who has overdosed.
- Ideally, observation should be performed by properly-trained professionals. This applies particularly where the overdose is due to the use of long-acting opioids. The period of observation needed to ensure full recovery is at least two hours, following overdose from short-acting opioids such as heroin. It may be longer where a longer acting opioid has been consumed.
- If a person relapses into opioid overdose, further naloxone administration may be required.
- The definition of "fully recovered" is a return to pre-overdose levels of consciousness two hours after the last dose of naloxone.
- After the overdose has been reversed, the person who has overdosed should be reminded not to use opioids and other drugs that will interfere with their recovery from the overdose.

- It is important to ensure that the person who is resuscitated understands what happened and the risks of what might happen next. It should also be recognized that this is "a teachable moment" – an opportunity to offer discussion of a range of treatment options and to train the person in the prevention and management of any future overdoses.

Decision on Strength of Recommendation

The GDG determined that this should be a strong recommendation despite the low quality of evidence due to the ethical barriers to testing this with randomized control trials. The GDG is aware that the short half-life of naloxone, coupled with difficulty ascertaining the dose and type of opioid taken, means that naloxone may cease to be effective before the person has fully recovered but the simple nature of the proposed intervention is unlikely to result in any harm, and the willingness of people likely to witness an overdose to remain with people who have overdosed is documented.

Definitions:

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group Grades of Evidence

High quality: Further research is very unlikely to change confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.

Very low quality: The Guideline Development Group is very uncertain about the estimate.

Strength of Recommendation

- Strong: The Guideline Development Group (GDG) was confident that the evidence of effect, combined with certainty about the values, preferences, benefits and feasibility, made this a recommendation that should be applied in most circumstances and settings.
- Conditional: There was less certainty about the evidence of effect and values, preferences, benefits and feasibility of this recommendation. Thus there may be circumstances or settings in which the recommendation does not apply.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Opioid overdose

Guideline Category

Counseling

Evaluation

Management

Prevention

Treatment

Clinical Specialty

Emergency Medicine

Family Practice

Internal Medicine

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Emergency Medical Technicians/Paramedics

Health Care Providers

Nurses

Other

Physician Assistants

Physicians

Public Health Departments

Social Workers

Substance Use Disorders Treatment Providers

Guideline Objective(s)

- To reduce the number of deaths from opioid overdose by providing evidence-based recommendations on the availability of naloxone for people likely to witness an opioid overdose along with advice on the resuscitation and post-resuscitation care of opioid overdose in the community
- To increase the availability of naloxone to people likely to witness an opioid overdose in the pre-hospital setting
- To increase the preparedness of people likely to witness an opioid overdose to respond safely and effectively by carrying naloxone and being trained in the management of opioid overdose
- To increase the rate of effective resuscitation and post-resuscitation care by persons witnessing an opioid overdose

Target Population

People at risk of opioid overdose and those likely to witness an opioid overdose in the community

Interventions and Practices Considered

1. Naloxone distribution to people who are likely to witness opioid overdose
2. Formulation, route of administration, and dose of naloxone
3. Resuscitation, focused on ventilation
4. Post-resuscitation care

Major Outcomes Considered

- Overdose mortality
- Overdose complication (such as aspiration)
- Overdose morbidity (prolonged adverse outcome of opioid overdose)

- Time to administer naloxone
- Time to opioid overdose reversal
- Opioid withdrawal reaction to naloxone
- Blood borne virus (BBV) transmission through unsafe injection
- Unsafe injection related injury
- Adverse effect of resuscitation
- Psychosocial intervention/referral to treatment post overdose
- Ease of administration
- Aggression directed towards the person encouraging observation by the overdose victim
- Second overdose event within 24 hours

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Systematic Evidence Search and Retrieval

The seven key questions governed the search strategy for the systematic reviews. There was considerable overlap in the areas to be searched, so for efficiency the strategy for searching the medical-literature databases for each of the reviews was combined and the inclusion and exclusion criteria were applied separately by the persons reviewing the results of the database search (see Annex 1 in the original guideline document for details of the search strategy).

To obtain reliable estimates of effect for the different population, intervention, comparison, outcome (PICO) questions, it was agreed that eligible studies be limited to randomized controlled trials (RCTs) or controlled prospective studies published in peer-reviewed journals, or presented as abstracts at scientific conferences, between 1 January 1966 and 1 January 2014.

Search Methods

Electronic Searches

The following electronic databases were searched:

- Medline (1966 to present)
- EMBASE (1980 to present)
- Cochrane library
- World Health Organization (WHO) library (2000 to present)
- Clinicaltrials.gov
- International Clinical Trials Registry Platform
- PsycINFO (1980 to present)
- CINAHL (1982 to present)
- Toxline (1965 to present)

Data Collation and Extraction

Selection of Studies

The initial screening was carried out by a single reviewer who inspected the search hits by reading titles and abstracts. Following this, each potentially relevant study located in the search was obtained in full text and assessed for inclusion independently by two reviewers. In doubtful or controversial cases, all identified discrepancies were discussed in order to reach consensus on all items.

Citations identified through computer database searching were initially screened into the following categories:

Yes – for articles clearly meeting the inclusion criteria for the review.

Pull to check – for articles which may meet the inclusion criteria; the full text of the article must be reviewed before final decision about inclusion can be made.

No – for articles clearly not meeting the inclusion criteria for the review; no further consideration is necessary.

Other Evidence Referred to in the Guidelines

Additional scientific literature is referred to in the guidelines to provide background and contextual information, and to assist in the completion of the balance between benefits and harms, values and preferences, and feasibility sections of the "evidence to recommendations" profiles. This evidence was not searched for systematically.

A separate online survey and key informant interviews were also conducted to inform the values and preferences section (see Annex 6 in the original guideline document).

Number of Source Documents

The search identified 5597 articles. These were screened by a single researcher, yielding 512 potentially relevant studies. Further screening by two researchers independently (disagreement resolved by discussion) reduced these to 29 relevant studies. Three researchers, including a Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodologist, independently screened and agreed on the final three included studies. See Figure 1 in the original guideline documents for a study selection flow diagram.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group Grades of Evidence

High quality: Further research is very unlikely to change confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.

Very low quality: The Guideline Development Group is very uncertain about the estimate.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data analysis was conducted using Review Manager (RevMan) Version 5.2 (The Nordic Cochrane Centre, Copenhagen) and GRADEprofiler (GRADEpro) version 3.6 (the GRADE working group). Where there was no effect size or studies could not be assessed using GRADEpro a narrative summary of the evidence was provided (see summaries in Annexes 2, 3, 4, and 5 in the original guideline document).

The quality of the evidence retrieved was assessed using Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. GRADE evidence profiles were developed for each key question, summarizing the quality of the evidence, a narrative assessment of benefits versus risks and harms, the estimated values and preferences of those who might be affected by the guidelines, and the costs, resource utilization and feasibility of the proposed interventions. Where necessary, these narrative descriptions also referred to other relevant evidence, not included in the systematic reviews, including one interrupted time-series analysis and 20 case series of programmes that had distributed naloxone, and five case series of opioid overdose recovery after naloxone. The characteristics of these studies and relevant outcomes are presented in

Annexes 2–5 in the original guideline document.

An online survey was conducted by the World Health Organization (WHO) to assess the values and preferences of those affected by the guidelines. This was completed by 661 respondents from 45 countries, including people at risk of opioid overdose, people with family members or friends who have overdosed or are at risk of opioid overdose, and people whose work brings them into contact with people who have experienced overdose and people at risk of overdose. A separate survey of 32 key informants was conducted by a consultant to the Department of HIV/AIDS, as part of a survey on human immunodeficiency virus (HIV) prevention, testing, treatment, harm reduction and community distribution of naloxone (see Annex 6 in the original guideline document for a detailed extract from the survey).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Individuals and Partners Involved in Development of the Guidelines

Members of the project's World Health Organization (WHO) Steering Group were drawn from Management of Substance Abuse, HIV, Essential Medicines and Health Products, Injury and Violence Prevention, Global TB Programme, and Service Delivery and Safety teams (see Annex 7 in the original guideline document for details).

The project's Guideline Development Group (GDG) was made up of content experts from all WHO regions, five of whom were female. A full list of members, their affiliations, expertise and countries is provided in Annex 7 of the original guideline document. Observers representing people at risk of opioid overdose and other stakeholder groups attended the GDG meeting in Geneva in February 2014, provided comments and technical information but did not participate in formulation of the recommendations. A full list of observers who attended the meeting and their affiliations is available in 'Acknowledgements' on page 5 in the original guideline document.

The GDG was supported by several consultants, three who performed the systematic reviews and provided all background documentation, and a fourth who advised on WHO guideline development methodology. A Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodologist reviewed the findings of the systematic review and developed the GRADE evidence profile (see Annex 8 in the original guideline document for details).

The External Review Group, whose members were drawn from people who may be affected by the guidance and people with content expertise, assessed all the evidence profiles and draft recommendations. The systematic reviewers and GDG considered their comments when finalizing the recommendations. A full list of external reviewers, their affiliations, countries, and expertise is provided in Annex 7 in the original guideline document.

How the Guidelines Were Developed

These guidelines were developed in accordance with the WHO Handbook for Guideline Development (see the "Availability of Companion Documents" field), and the process was overseen by the WHO Guidelines Review Committee. Development of the guidelines began in October 2013 with the establishment of the WHO Steering Group and the GDG which identified the key questions on which advice was needed. These questions were then formulated in PICO format (population, intervention, comparator, outcome). The GDG selected a list of outcomes for each PICO question and then ranked these by importance on a scale from 1 to 9. A ranking of 7–9 was considered 'critical', 4–6 'important' and 1–3 'not important'. Only critical and important outcomes were considered.

With the exception of the values-and-preferences survey and key-informant results, the GRADE profiles were circulated for external review prior to the face-to-face meeting of the GDG.

The guideline development meeting, held in Geneva (19–20 February 2014), was attended by GDG members and observers from organizations working with or representing people who use drugs, relevant professional societies, concerned government health agencies, intergovernmental organizations and WHO collaborating centres. Materials presented included GRADE evidence profiles, evidence summaries and systematic reviews, along with background documentation and findings from the values-and-preferences survey and key-informant interviews.

A GRADE decision table was used to guide the determination of the strength of each recommendation (strong or conditional), based on the quality of the evidence, whether benefits outweighed harms, whether values and preferences of guideline end-users favoured the recommendation, and whether or not the recommendation was feasible and cost-effective (see Annexes 2–5 in the original guideline document for the decision tables).

At the beginning of the meeting, the GDG agreed that decisions on the strength and wording of recommendations would preferably be reached by consensus – defined as a state where all members of the GDG agree with the wording of recommendations and accompanying comments. It was further agreed that when unanimous agreement could not be achieved, an open vote would be held and decisions carried by a simple majority (more than 50%). In the meeting, the wording of all recommendations was agreed by consensus, and voting was not required.

While discussing the recommendations, the GDG recommended that the scope of the guidelines be limited to pre-hospital care, enabling the guideline to be better targeted to opioid overdose in the community setting. This meant that several of the questions were no longer within the scope of the guideline and were therefore not discussed further at the meeting.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

- Strong: The Guideline Development Group (GDG) was confident that the evidence of effect, combined with certainty about the values, preferences, benefits and feasibility, made this a recommendation that should be applied in most circumstances and settings.
- Conditional: There was less certainty about the evidence of effect and values, preferences, benefits and feasibility of this recommendation. Thus there may be circumstances or settings in which the recommendation does not apply.

Cost Analysis

Costs and Resource Use

- The panel judged naloxone distribution and training interventions to be currently cost-effective across a range of economic settings for the treatment of opioid overdose in the community. Approximately 20% of doses distributed in observational studies are reported to be used. Naloxone was used in approximately 70% of the overdoses witnessed by laypersons provided with take-home naloxone. However, the panel noted that while naloxone is currently affordable, there is a possibility that new formulations targeted for community use will be developed, and that should the price rise considerably this may be a less cost-effective intervention. The panel noted the lack of analyses or modelling studies to guide assessment of the cost-effectiveness of take-home naloxone programmes for people using prescribed opioids.
- The panel judged the costs associated with the various routes of administration to be currently low, noting some uncertainty of the pricing of specifically designed products for lay administration currently under development.

Please refer to Annexes 2–5 in the original guideline document for more information regarding resource use.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

After the guideline development meeting, the draft recommendations and background systematic reviews were circulated to a group of external reviewers (see Annex 7 in the original guideline document for details). Revision of the draft recommendations and remarks was made if reviewers identified an issue that had not been considered at the guidelines meeting or proposed changes which improved the clarity of the text without changing the meaning. The revised recommendations were then circulated among the Guideline Development Group (GDG) members and proposed changes were accepted if agreed upon by the entire group.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Reduced number of deaths from opioid overdose. See the "Benefits and Harms" section for each recommendation for benefits of specific interventions.

Potential Harms

- The possibility of adverse effects (including prolonged opioid withdrawal and seizures) with the use of naloxone doses higher than 2 mg was considered a potential harm.
- The main adverse event associated with naloxone use for reversal of opioid intoxication is an acute opioid withdrawal syndrome, characterised by agitation and anxiety, nausea, myalgia and sweating.
- Adverse effects of resuscitation (e.g., chest injuries)
- The panel decided that there is a potential for harm from rebound opioid toxicity following reversal of opioid overdose with naloxone in the community if the person who has overdosed is left unsupervised. This risk of harm can be reduced considerably if the first responder remains with the person who has overdosed until after the effects of naloxone have "worn off" and monitors their breathing and level of consciousness.
- The only other adverse outcome described in the observational studies reviewed are seizures, occurring in 0.45% of cases (0.43% to 0.47%).

See the "Benefits and Harms" section for each recommendation for harms of specific interventions.

Qualifying Statements

Qualifying Statements

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Implementation of the Guideline

Description of Implementation Strategy

These recommendations will be used to provide guidance on the identification and management of opioid overdose in the community setting through a number of derivative publications, including model training materials and an implementation manual. These will be widely disseminated via the World Health Organization (WHO) regional and country offices, collaborating centres, professional organizations and partner agencies.

These recommendations will be adapted for the field by developing suitable training materials in consultation with regional, national and local stakeholders. Adaptation will include translation into appropriate languages and ensuring that the interventions are acceptable in local sociocultural contexts and suitable for local health systems.

Suggested measures for evaluating the impact of recommendations are provided in the original guideline document.

Implementation Tools

Audit Criteria/Indicators

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

World Health Organization (WHO). Community management of opioid overdose. Geneva (Switzerland): World Health Organization (WHO); 2014. 74 p. [133 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2014

Guideline Developer(s)

World Health Organization - International Agency

Source(s) of Funding

The World Health Organization (WHO) gratefully acknowledges the financial support of the Government of Norway and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) for the production of these guidelines.

Guideline Committee

World Health Organization (WHO) Steering Group

Guideline Development Group (GDG)

Composition of Group That Authored the Guideline

WHO Steering Group: Nicolas Clark, Management of Substance Abuse; Vladimir Poznyak, Management of Substance Abuse; Annette Verster, HIV; Elizabeth Mathai, Essential Medicines and Health Products; Margaret Peden, Injuries and Violence Prevention; Annabel Baddeley, Global TB Programme; Selma Khamassi, Service Delivery and Safety

Guideline Development Group: Robert Balster (*Chair*), Virginia Commonwealth University, United States of America; Barbara Broers, Hospital University Geneva, Switzerland; Jane Buxton, University of British Columbia/BC Centre for Disease Control, Canada; Paul Dietze, The Macfarlane Burnet Institute for Medical Research and Public Health, Australia; Kirsten Horsburgh, Scottish Drugs Forum National Naloxone Coordinator, Scotland, UK; Raka Jain, All India Institute of Medical Sciences – National Drug Dependence Treatment Centre, India; Nadeemullah Khan, Aga Khan University, Pakistan; Walter Kloek, Resuscitation Council of Southern Africa, South Africa; Emran Razzaghi, University of Tehran, Iran; Hendry Sawe, Muhimbili National Hospital, Tanzania; John Strang, King's College London, England, UK; Oanh Thi Hai Khuat, SCDI – Center for Supporting Community Development Initiatives, Vietnam

External Reviewers: Sophia Achab, University Hospital of Geneva, Switzerland; Luis Isidoro Alfonzo Bello, Pan American Health Organization, United States of America; Sawitri Assanangkorchai, Prince of Songkla University, Thailand; Marc Augsburger, The International Association of Forensic Toxicologists, Switzerland; Regis Bedry, European Association of Poisons Centres and Clinical Toxicologists, France; Scott Burris, Tempe University School of Law, United States of America; Edward Day, Birmingham Medical Trust, England, UK; Gail D'Onofrio, Yale School of Medicine, United States of America; Ali Farhoudian, Substance Abuse and Dependence Research Centre, Iran; Evgeny Krupitsky, St Petersburg Psychoneurological Institute, Russia; Soraya Mayet, Durham University, England, UK; Dasha Ocheret, Eurasian Harm Reduction Network, Lithuania; Shahin Shadnia, Shahid Beheshti University of Medical Sciences, Iran; Sharon Stancliff, Harm Reduction Coalition, United States of America; David Sugerman, Centers for Disease Control and Prevention, United States of America; Ambros Uchtenhagen, Addiction Research Institute, Switzerland; Alexander Walley, Virginia Commonwealth University, United States of America; Sharon Walsh, University of Kentucky, United States of America

Financial Disclosures/Conflicts of Interest

All Guideline Development Group (GDG) members, external reviewers and consultants completed the World Health Organization (WHO) Declaration of Interest forms. Several GDG members declared academic and financial interests. These were then reviewed by the secretariat for potential conflicts of interest. Where conflicts of interest were assessed as potentially serious, they were referred to the WHO legal department (see summary in Annex 8 in the original guideline document). The declared interest of Bob Balster (Chair) was determined not to represent a conflict for these guidelines. Two GDG members were assessed to have a serious conflict of interest. Raka Jain's conflict was assessed as serious as she had received funding from Rusan Pharmaceuticals, a manufacturer of naloxone, although it was for work on an unrelated product. John Strang's conflict was considered serious because his organization had received funding from Martindale, a manufacturer of naloxone, even though the funding was for work on an unrelated product, and because of his current work on a non-injectable formulation of naloxone. Both were excluded from participation in discussions and decisions relating to the use and availability of naloxone. The remaining conflicts of interest were not considered serious and thus all other GDG members were able to participate in all decisions.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the World Health Organization (WHO) Web site .

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: bookorders@who.int.

Availability of Companion Documents

The following are available:

- Information sheet on opioid overdose. 2014 Nov. Available from the World Health Organization (WHO) Web site .
- WHO handbook for guideline development. Geneva (Switzerland): World Health Organization (WHO); 2012. 56 p. Electronic copies: Available from the WHO Web site .

In addition, suggested measures for evaluating the impact of recommendations are provided in the original guideline document .

Patient Resources

None available

NGC Status

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